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Health-Related Quality of Life in I-125 Prostate Brachytherapy Patients Treated with and without Volume-Reducing Hormone Therapy: Results of a Short-Term Prospective Study

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Abstract

Purpose: This study describes the differences in short-term effects of health-related quality of life (HRQOL) in I-125 prostate brachytherapy patients who were treated with and without volume-reducing hormone therapy.
Patients and Methods: Prostate cancer patients (N = 312) filled out questionnaires on HRQOL (European Organization of Research and Treatment of Cancer Quality of Life Questionnaire [EORTC-QLQ]-C30 and EORTC-QLQ-PR25) before treatment and 6 weeks and 3 months after treatment. HRQOL was compared between the two groups: Patients who were receiving brachytherapy (n = 233) and patients who were receiving brachytherapy with volume-reducing hormone therapy (n = 79). Duration of androgen ablation was 9 months, starting 3 months before I-125 implantation.
Results: After treatment, patients reported significant and clinically relevant decreased scores on the following subscales: Global health status, role functioning, social functioning, pain, insomnia, bowel symptoms and functioning, and treatment-related functions, regardless of the therapy they received. Results showed that prostate cancer patients receiving brachytherapy with volume-reducing hormone therapy also experienced lower treatment-related functions and lower sexual function. Significant time by treatment interaction effects were found for treatment-related functions. The subscale treatment-related functions was the only scale that showed a difference over time, between treatments, and time by treatment.
Conclusions: The differences in HRQOL between brachytherapy and brachytherapy with volume-reducing hormone therapy are small; they both decrease HRQOL and increase treatment-related problems. A long-term prospective study on long-term effects on HRQOL is needed to obtain a more comprehensive view of the consequences of a specific treatment modality over time. Our results can help to identify the problems patients face after brachytherapy with or without hormone therapy; these problems deserve additional attention during the period of recovery.

Introduction

Prostate cancer is the most common malignancy in men in the western world.[1] In 2005, 9,500 men in the Netherlands received a diagnosis of prostate cancer, and this number is expected to increase to 15,000 by the year 2015.[2] Brachytherapy is one of the treatment options for localized prostate cancer. Sometimes brachytherapy patients undergo volume-reducing hormone therapy because of a large prostate volume or high-risk tumor characteristics (eg, high prostate-specific antigen [PSA] levels, high Gleason scores, or a high tumor stage).

Prostate cancer can affect general health-related quality of life (HRQOL) (e.g., physical, psychological, and social func-

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tioning) and disease-specific HRQOL (eg, urinary, sexual, and bowel functioning).[3–6] Differences in effects on HRQOL between treatment methods exist. In this study, we compared "brachytherapy" with "brachytherapy with volume-reducing hormone therapy" on HRQOL aspects.

Urinary complaints after prostate brachytherapy are common but only rarely severe.[7] Moreover, they appear to peak 1 month after brachytherapy and subsequently return to their baseline values after 1 year.[8] Compared with a control group of patients with prostate cancer who were not treated, brachytherapy patients did not differ in overall urinary HRQOL at follow-up (mean = 26 months).[9] Another study, however, found that during a 4-year period (2.6 years to 6.2 years after treatment), urinary incontinence worsened in patients treated with brachytherapy.[6]

Patients receiving hormone therapy only reported more physical discomfort 1 year after diagnosis compared with men who did not receive hormone therapy.[10] Furthermore, among men who were sexually potent before diagnosis, 80% of patients treated with hormone therapy reported being impotent after one year.[10] In addition, patients who had received hormone therapy reported reduced energy, and poorer sexual and urinary function; they were more bothered by their urinary and sexual function than patients undergoing radical prostatectomy or radiotherapy.[5] Patients treated with hormone therapy for at least 12 months had osteoporosis, unfavorable body composition, sexual dysfunction, and reduced overall HRQOL scores.[11]

To summarize, both brachytherapy and hormone therapy appear to have a negative influence on HRQOL. To the best of our knowledge, however, only one study has been published that compared HRQOL between prostate cancer patients treated with brachytherapy versus brachytherapy with volume-reducing hormone therapy.[12] Compared with patients treated with brachytherapy, brachytherapy with volume-reducing hormone therapy led to lower HRQOL in all domains 29 months after treatment. This was significant and clinically relevant for urinary bother, sexual function/bother, and hormone function/bother. Despite its relevance, that study was cross-sectional and could therefore not register changes between treatments over time. Therefore, we examined the short-term influence of brachytherapy and brachytherapy with volume-reducing hormone therapy on HRQOL in patients with T_1-T_2 prostate cancer in a prospective study.

Patients and Methods

Setting and participants

This study was conducted at the Catharina Hospital, Eindhoven, the Netherlands. A total of 386 patients who had received a diagnosis of T_1-T_2 prostate cancer in the period between July 2000 and November 2004 were asked to participate in this study.

All patients were treated with I-125 prostate brachytherapy. Brachytherapy was often applied with volume-reducing hormone therapy to reduce the volume of the prostate in patients with prostate gland volume >60 cc or to exterminate the influence of testosterone on the tumor in high-risk patients.[13] A majority was treated with a combination of antiandrogen and LHRH (luteinizing hormone-releasing hormone) analogues (70%), some were treated with only antiandrogens (19%), and some were treated with only LHRH analogues (11%) (Table 1). Duration of androgen ablation was 9 months, starting 3 months before I-125 implantation.

Data collection

Patients were asked to complete our measure at three points in time: Before treatment (T1), 6 weeks after the start of treatment (T2), and 3 months after treatment (T3). Thus, in the case of patients treated with brachytherapy only, they received the first questionnaire before brachytherapy. In the case of patients treated with brachytherapy with volume-reducing hormone therapy, they received the first questionnaire before the start of hormone therapy and thus 3 months before brachytherapy. Measurements two and three were similar in both groups—namely 6 weeks and 3 months after brachytherapy.

Patients were reassured that nonparticipation did not have any consequences for their follow-up care or treatment. Returned questionnaires only contained a study number that guaranteed anonymity. The Medical Ethics Committee of Catharina Hospital approved this study. Written informed consent was obtained from every patient after the study procedure had been fully explained.

Measures

Patient data, including age, tumor-node-metastasis-classification,[14] pretreatment PSA, Gleason score, grade, and primary treatment were derived from patients' medical records.

The European Organization of Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC-QLQ-C30) version 3.0 was used to measure global HRQOL.[15] This questionnaire contains five functional scales (physical, role, emotional, cognitive, and social functioning), a global HRQOL scale, three symptom scales (nausea and vomiting, fatigue, and pain), and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties).

Urologic, bowel, and sexual functioning were measured with the EORTC-QLQ PR25.[16] This questionnaire contains five scales (urinary problems, bowel symptoms and functioning, treatment-related functions, sexual functioning, and sexual activity).

The response format of the EORTC-QLQ-C30 and the EORTC-QLQ-PR25 was a Likert scale. According to standard scoring procedures, all scales were linearly converted to a 0 to 100 scale, with higher scores indicating better functioning.

Statistical analyses

The Statistical Package for the Social Sciences (SPSS 12.0.0 for Windows) was used for all data analyses. Patient characteristics and clinical parameters were described in percentages and were analyzed using chi-square tests for categorical variables.

Linear regression analyses were carried out to investigate the association between patient characteristics (age, stage, grade, pretreatment PSA and Gleason score) with the subscale scores of the EORTC-QLQ-C30 and EORTC-QLQ-PR25. On the basis of the univariate results, multivariate models were constructed to determine which of the patient and tumor characteristics were associated independently with

HRQOL outcomes. We controlled for these variables in the analysis of variance (general linear repeated-measures model), which was used to compare HRQOL scores between patients treated with brachytherapy or brachytherapy with volume-reducing hormone therapy, at three points in time.

P values are presented for within-subjects effects over time (before treatment and 6 weeks and 3 months after treatment), between-subjects effects for treatment (brachytherapy or brachytherapy with volume-reducing hormone therapy), and time by treatment interaction effects. These *P* values are all Greenhouse-Geisser corrected except for the subscale constipation, where sphericity was assumed. *P* values less than 0.01 were considered statistically significant and are included in the text. *P* values less then 0.05 are only mentioned in the tables. We used Norman's "rule of thumb" that the threshold of discrimination for clinically relevant changes in HRQOL for a chronic disease appears to be approximately half a standard deviation.[17]

Results

Sociodemographic characteristics

Three hundred and twelve (81%) of the 386 suitable prostate brachytherapy patients returned a completed questionnaire at least once (Table 1). Before treatment, 295 patients (17 missing) returned the set of questionnaires; 6 weeks after treatment, 266 patients (46 missing) returned questionnaires; and 3 months after treatment, 263 patients (49 missing) returned questionnaires. All of them underwent I-125 brachytherapy, and 79 of them also underwent volume-reducing hormone therapy. No statistically significant differences in age at the time of the survey, Gleason score, pretreatment PSA, stage, and grade were found between both treatment groups.

Table 1. Sociodemographic and Medical Characteristics of Patients Treated with Brachytherapy with or without Hormonal Therapy

	Brachytherapy n = *233* n *(%)*	*Brachytherapy in combination with hormones* n = *79* n *(%)*	P *value*
Age at time of survey (years)			
41–50	5 (2)	1 (1)	0.50
51–60	51 (22)	12 (15)	
61–70	119 (51)	47 (60)	
70+	58 (25)	19 (24)	
Gleason			
2–4	26 (11)	10 (13)	0.80
5–7	203 (87)	69 (87)	
8	1 (0)	0 (0)	
Unknown	3 (1)	0 (0)	
PSA ng/mL (pretreatment)			
1–5	59 (25)	15 (19)	0.62
6–10	117 (50)	43 (54)	
11–15	36 (16)	12 (15)	
16–20	12 (5)	5 (6)	
21–25	3 (1)	3 (4)	
25+	5 (2)	1 (1)	
Missing values	1 (0)	0 (0)	
Stage			
T_{1c}	133 (57)	50 (63)	0.67
T_{2a}	65 (28)	21 (27)	
T_{2b}	11 (5)	2 (3)	
T_{2c}	24 (10)	6 (8)	
Grade[a]			
1	28 (12)	10 (13)	0.79
2	189 (81)	67 (85)	
3	2 (1)	0 (0)	
Missing values	14 (6)	2 (3)	
Primary treatment			
Brachytherapy	233 (100)	0 (0)	
Brachytherapy + antiandrogens + LHRH-analogues	0 (0)	55 (70)	
Brachytherapy + antiandrogens	0 (0)	15 (19)	
Brachytherapy + LHRH-analogues	0 (0)	9 (11)	

[a]Grade was based on the tumor-node-metastasis clinical classification.[14] Grade 1 is comparable to a Gleason score of 2 to 4, grade 2 is comparable to a Gleason score of 5 to 7, and grade 3 is comparable to a Gleason score of 8 to 10.

PSA = prostate-specific antigen; LHRH = luteinizing hormone-releasing hormone.

Differences in HRQOL over time

EORTC-QLQ-C30 subscale scores in both patient groups changed significantly between the three measurements. Globally, scores decreased after treatment, increased again between 6 weeks and 3 months after treatment, but never reached the pretreatment level again. Statistically significant and clinically relevant differences[17] between measurements 1, 2, and 3 were found for global health status ($P < 0.001$), role functioning ($P < 0.001$), social functioning ($P < 0.001$), fatigue ($P < 0.001$), pain ($P < 0.001$), and insomnia ($P < 0.001$). For example, values for the subscale global health status decreased significantly 6 weeks after treatment, but after 3 months, the self-reported global health status improved again for both treatment groups.

Scores on the EORTC-QLQ-PR25 showed a similar pattern; they decreased after treatment, followed by an increase between 6 weeks and 3 months after treatment, but they also failed to reach pretreatment levels. Repeated measures showed significant and clinically relevant decreases over time for the subscales bowel symptoms and functioning ($P < 0.001$), and treatment-related functions ($P < 0.001$). These findings demonstrate an increase of these prostate cancer-related complaints, regardless of the treatment. Incontinence aids were used by too few respondents, so they were discarded from analysis.

Differences in HRQOL between treatment methods

Statistically significant effects for treatment (brachytherapy *versus* brachytherapy with volume-reducing hormone therapy) were not found for the subscales of the EORTC-QLQ-C30.

For the EORTC-QLQ-PR25, statistically significant and clinically relevant differences between the two treatment methods were found for the subscales treatment-related functions ($P < 0.001$) and sexual functioning ($P < 0.001$). The average scores for the significant subscales were lower for patients who received brachytherapy with volume-reducing hormone therapy compared with patients who were treated with brachytherapy only.

Differences in HRQOL over time for treatment methods

Significant time by treatment interaction effects for the subscales of both questionnaires was only found for treatment-related functions ($P < 0.001$). It appeared that a greater reduction in HRQOL was found over time on this subscale when receiving brachytherapy with volume-reducing hormone therapy in contrast to treatment with brachytherapy only.

Discussion

This study examined the short-term influence of brachytherapy and brachytherapy with volume-reducing hormone therapy on HRQOL in patients with T_1-T_2 prostate cancer in a prospective study. Both brachytherapy and brachytherapy with volume-reducing hormone therapy negatively influenced HRQOL (global health status, role functioning, social functioning, pain, insomnia) and caused treatment-related problems (bowel symptoms and functioning, treatment-related functions, and sexual functioning) 6 weeks and 3 months after treatment. The differences in HRQOL between brachytherapy and brachytherapy with volume-reducing hormone therapy were small.

To date, no prospective studies have been published that have as a primary objective to compare HRQOL over time between patients treated with either brachytherapy or brachytherapy with volume-reducing hormone therapy. Therefore, our results are difficult to compare with previous findings. A recent prospective study among T_1 and T_2 prostate cancer patients, however, concluded that those treated with brachytherapy reported having long-lasting urinary irritation, bowel and sexual symptoms, and transient problems with vitality or hormone function. Furthermore, adjuvant hormone therapy was associated with worse outcomes across multiple quality-of-life domains among patients who were receiving brachytherapy.[18] Despite the fact that comparing brachytherapy patients treated with and without volume-reducing hormone therapy was not the objective of that study and despite the fact that different questionnaires were used, it partly confirms our results.

A Dutch study among 127 patients with low-stage prostate cancer who were treated with brachytherapy that did use the same questionnaires also found a decrease in HRQOL 4 weeks after treatment.[19] One year after implant, HRQOL of the patients was at least equal to preimplant scores, which suggests that many of the negative effects may recover in the long term. This confirms the reports that demonstrate that acute side effects after brachytherapy for prostate cancer appear to peak 1 month after brachytherapy and subsequently return to their baseline values at 1 year.[8] In addition, after brachytherapy, dysuria is a relatively common complaint, but at approximately 45 months after therapy, it appears to have been resolved in almost all patients.[7]

According to a Japanese study, morbidity (associated with brachytherapy followed by external beam radiotherapy) was highest during the first month of treatment, and it affected HRQOL significantly. Most outcome measures, however, showed a recovery to baseline levels 12 months after radiation therapy.[20] Finally, a Swedish study on HRQOL after external beam radiotherapy and brachytherapy revealed that the negative contribution from neoadjuvant androgen deprivation therapy on symptom development seemed to be substantial but mostly transitory.[21]

Our study also showed a decrease in HRQOL after treatment followed by an increase between 6 weeks and 3 months after treatment. Unlike the studies described above, however, our HRQOL scores failed to reach the pretreatment level again within 3 months. This period is probably too short to show a complete recovery. An additional follow-up measurement to this study (>1 year after treatment) could possibly demonstrate a complete recovery in HRQOL.

Patient-reported analyses of the effects of volume-reducing hormone therapy on HRQOL after brachytherapy are scarce. Only one German study compared HRQOL in prostate cancer patients (n = 134) who were treated with only brachytherapy with patients who received brachytherapy with volume-reducing hormone therapy.[12] That study reported lower HRQOL on all domains of the Expanded Prostate Cancer Index questionnaire in patients who were treated with brachytherapy with volume-reducing hormone therapy compared with patients who were treated with brachytherapy only. Two major drawbacks of that study,

Table 2. Mean Scores on FORTC-QLQ-C30 and EORTC-QLQ-PR25 Subscales at Three Time Points Before Treatment (T1), 6 Weeks after Treatment (T2), and 3 Months after Treatment (T3) for Brachytherapy (b) or Brachytherapy in Combination with Volume-Reducing Hormone Therapy (b + h)

	T_1		T_2		T_3				
	b n = *221* *Mean (SD)*	*b + h* n = *73* *Mean (SD)*	*b* n = *193* *Mean (SD)*	*b + h* n = *71* *Mean (SD)*	*b* n = *197* *Mean (SD)*	*b + h* n = *64* *Mean (SD)*	P *value* *Time*	P *value* *Treatment*	P *value* *Time* treatment*
EORTC QLQ-C30									
Global health status	80 (16)	81 (14)	72 (20)	69 (22)	74 (19)	72 (20)	<0.001	NS	NS
Physical functioning	93 (11)	93 (9)	89 (15)	85 (16)	90 (14)	84 (18)	<0.05	NS	<0.05
Role functioning	92 (18)	90 (20)	79 (25)	76 (28)	82 (24)	78 (26)	<0.001	NS	NS
Emotional functioning	82 (20)	88 (15)	84 (21)	85 (18)	85 (21)	86 (17)	NS	NS	NS
Cognitive functioning	91 (14)	89 (15)	90 (14)	85 (21)	90 (15)	84 (21)	<0.05	<0.05	NS
Social functioning	92 (15)	92 (13)	86 (21)	79 (26)	87 (20)	80 (25)	<0.001	NS	NS
Fatigue	89 (17)	84 (16)	77 (23)	72 (25)	80 (22)	73 (23)	<0.001	<0.05	NS
Nausea and vomiting	100 (3)	99 (4)	97 (8)	98 (6)	98 (7)	98 (5)	NS	NS	NS
Pain	92 (15)	93 (16)	81 (25)	81 (27)	83 (24)	79 (25)	<0.001	NS	NS
Dyspnea	91 (9)	93 (7)	89 (21)	89 (20)	89 (22)	84 (24)	<0.05	NS	<0.05
Insomnia	87 (25)	86 (21)	79 (26)	73 (34)	83 (24)	76 (30)	<0.001	NS	NS
Appetite loss	98 (11)	95 (16)	95 (15)	95 (15)	96 (14)	94 (16)	NS	NS	NS
Constipation	95 (14)	94 (14)	90 (22)	87 (23)	92 (21)	90 (18)	NS	NS	NS
Diarrhea	94 (15)	97 (10)	89 (20)	86 (22)	88 (21)	90 (17)	NS	NS	NS
Financial difficulties	98 (11)	99 (6)	96 (13)	98 (9)	96 (13)	98 (8)	NS	NS	NS
EORTC QLQ-PR25									
Urinary problems	84 (18)	82 (15)	61 (22)	55 (17)	63 (22)	59 (20)	NS	NS	NS
Incontinence aids[a]	92 (17)	89 (19)	92 (17)	78 (19)	92 (17)	78 (19)	NS	NS	NS
Bowel symptoms and functioning	96 (9)	95 (8)	91 (11)	88 (11)	90 (13)	88 (11)	<0.001	NS	NS
Treatment related functions	94 (9)	91 (10)	92 (11)	81 (15)	92 (10)	80 (15)	<0.001	<0.001	<0.001
Sexual functioning	38 (24)	29 (22)	28 (21)	16 (23)	31 (21)	18 (23)	<0.05	<0.001	NS
Sexual activity	78 (20)	68 (22)	61 (22)	50 (24)	58 (21)	49 (21)	<0.05	<0.05	NS

[a]Incontinence aids were used by too few respondents (7 total) to be statistically significant.

All scales were linearly converted to a 0 to 100 scale, with higher scores indicating better functioning.

P values are given for the effects of time, treatment, and time * treatment. *P* values less than 0.01 were considered statistically significant and are included in the text. *P* values less then 0.05 are only mentioned in the tables.

EORTC QLQ-PR25 = tumor-specific European Organization for Research and Treatment of Cancer prostate cancer module; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer core questionnaire; SD = standard deviation; NS = not significant.

however, were its cross-sectional nature and the fact that it compared HRQOL 2 to 50 months after treatment.

In our study, we did not find a HRQOL difference in all domains between the two treatments. It appeared that prostate cancer patients who received brachytherapy with volume-reducing hormone therapy experienced more negative effects of their treatment (lower treatment-related functions and worse sexual functioning) compared with patients who were treated with brachytherapy only. Comparison of the findings of both studies is not possible, given the different questionnaire and the substantial difference in the timing of the measures.

Other studies[22–24] that compared both treatment groups did not include HRQOL measures. Potency rates decreased significantly after brachytherapy with volume-reducing hormone therapy compared with brachytherapy alone 5 years after treatment (76% *versus* 52%).[22] Furthermore, rectal function after brachytherapy with volume-reducing hormone therapy was slightly worse than after brachytherapy only. This difference, however, did not reach statistical significance.[23] Finally, volume-reducing hormone therapy was found to be associated with an significantly increased risk of urinary retention.[24]

Sexual functioning was both statistically worse in patients in the volume-reducing hormone therapy group before treatment compared with the brachytherapy only group. The difference in sexual functioning, however, between patients treated with or without volume-reducing hormone therapy was probably not related to therapy, because a statistically significant difference was already present before the onset of therapy. The fact that sexual functioning was not significant in the "time by treatment analysis" confirms this idea. The subscale treatment-related functions was the only scale that showed a difference over time, between treatments, and time by treatment.

The present study has some limitations. First, maybe not all hormone treatments are comparable. In this study, the majority of patients were treated with antiandrogen or LHRH analogues, or a combination of both (89%). There were patients (11%) who received other hormone therapies, such as cyproterone acetate or leuprorelin acetate. These therapies may have a different effect on HRQOL. This could not be evaluated in this study because of the low number of patients receiving these treatments.

In addition, comorbidity is a factor that can influence HRQOL and is therefore often controlled for in HRQOL studies.[25–27] Comorbidity might also interfere with our results and is not corrected for in this research, because information on comorbidity was not available. We have no reason to suspect, however, that comorbidity is present more in either treatment group.

Finally and most importantly, the current study only focused on relatively short-term effects (up to 3 months). It is possible that, after treatment, patients who were treated with hormone therapy report a lower HRQOL because they are still bothered by the effects of hormone therapy, which wear off more slowly compared with the treatment effects of brachytherapy. A long-term prospective study on long-term effects on HRQOL is needed to obtain a more comprehensive view of the consequences of a specific treatment modality over time.

Conclusion

We think that the results of this study add importantly to the limited information available on HRQOL in patients with prostate cancer who receive brachytherapy or brachytherapy with volume-reducing hormone therapy, especially because of its prospective nature. Insight into the effects of brachytherapy on HRQOL is important as this therapy becomes more standard in the treatment of men with early-stage prostate cancer.

The differences in HRQOL in patients who are treated with brachytherapy or brachytherapy with volume-reducing hormone therapy are small. Both treatments cause a decrease in HRQOL and increase in treatment-related problems. Our results can help to identify the problems patients face after brachytherapy with or without hormone therapy; these problems deserve additional attention during the period of recovery. Long-term prospective studies on the long-term effects on HRQOL are needed, however, to obtain a more comprehensive view of the consequences of a specific treatment modality over time.

Disclosure Statement

No competing financial interests exist.

References

1. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. Eur J Cancer 2001;37(suppl 8): S4–S66.
2. Signaleringscommissie-Kanker, Kanker in Nederland. Trends, prognoses en implicaties voor zorgvraag. [Cancer in the Netherlands. Trends, prognosis and implications for health care.]. Amsterdam: KWF Kankerbestrijding, 2004.
3. Clark JA, Inui TS Silliman RA, Bokhour BG, Krasnow, SH, Robinson RA, Spaulding M, Talcott JA. Patients' perceptions of quality of life after treatment for early prostate cancer. J Clin Oncol 2003;21: 3777–3784.
4. Wei JT, Dunn RL, Sandler HM, McLaughlin PW, Montie JE, Litwin MS, Nyquist L, Sanda MG. Comprehensive comparison of health-related quality of life after contemporary therapies for localized prostate cancer. J Clin Oncol 2002;20: 557–566.
5. Lubeck DP, Grossfeld GD, Carroll PR. The effect of androgen deprivation therapy on health-related quality of life in men with prostate cancer. Urology 2001;58(suppl 1):94–100.
6. Miller DC, Sanda MG, Dunn RL, Montie JE, Pimentel H, Sandler HM, McLaughlin WP, Wei JT. Long-term outcomes among localized prostate cancer survivors: Health-related quality-of-life changes after radical prostatectomy, external radiation, and brachytherapy. J Clin Oncol 2005;23:2772–2780.
7. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Murray B, Zeroski D, Lief JH. Dysuria after permanent prostate brachytherapy. Int J Radiat Oncol Biol Phys 2003;55:979–985.
8. Cesaretti JA, Stone NN, Stock RG. Urinary symptom flare following I-125 prostate brachytherapy. Int J Radiat Oncol Biol Phys 2003;56:1085–1092.
9. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Lief JH. Long-term urinary quality of life after permanent prostate brachytherapy. Int J Radiat Oncol Biol Phys 2003;56:454–461.
10. Potosky AL, Reeve BB, Clegg LX, Hoffman RM, Stephenson RA, Albertsen PC, Gilliland FD, Stanford JL. Quality of life

following localized prostate cancer treated initially with androgen deprivation therapy or no therapy. J Natl Cancer Inst 2002;94:430–437.
11. Basaria S, Lieb J II, Tang QAM, DeWeese T, Carducci M, Eisenberger M, Dobs AS. Long-term effects of androgen deprivation therapy in prostate cancer patients. Clin Endocrinol (Oxf) 2002;56:779–786.
12. Pinkawa M, Fischedick K, Gagel B, Piroth MD, Borchers H, Jakse G, Ebie MJ. Association of neoadjuvant hormonal therapy with adverse health-related quality of life after permanent iodine-125 brachytherapy for localized prostate cancer. Urology 2006;68:104–109.
13. Lee LN, Stock RG, Stone NN. Role of hormonal therapy in the management of intermediate- to high-risk prostate cancer treated with permanent radioactive seed implantation. Int J Radiat Oncol Biol Phys 2002;52:444–452.
14. UICC. TNM Atlas: Illustrated Guide to the TNM/pTNM Classification of Malignant Tumors. Berlin: SpringerVerlag, 1992, pp 141–144.
15. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993;85:365–376.
16. Borghede G, Sullivan M. Measurement of quality of life in localized prostatic cancer patients treated with radiotherapy. Development of a prostate cancer-specific module supplementing the EORTC QLQ-C30. Qual Life Res 1996;5:212–222.
17. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: The remarkable universality of half a standard deviation. Med Care 2003;41: 582–592.
18. Sanda MG, Dunn RL, Sandler HM, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. N Engl J Med 2008;358:1250–1261.
19. Van Gellekom MP, Moerland MA, Van Vulpen M, Wijrdeman HK, Battermann JJ. Quality of life of patients after permanent prostate brachytherapy in relation to dosimetry. Int J Radiat Oncol Biol Phys 2005;63:772–780.
20. Egawa S, Shimura S, Irie A, Kitano M, Nishiguchi I, Kuwao S, Hayakawa K, Baba S. Toxicity and health-related quality of life during and after high dose rate brachytherapy followed by external beam radiotherapy for prostate cancer. Jpn J Clin Oncol 2001;31:541–547.
21. Wahlgren T, Brandberg Y, Häggarth L, Hellström M, Nilsson S. Health-related quality of life in men after treatment of localized prostate cancer with external beam radiotherapy combined with (192)ir brachytherapy: A prospective study of 93 cases using the EORTC questionnaires QLQ-C30 and QLQ-PR25. Int J Radiat Oncol Biol Phys 2004;60:51–59.
22. Potters L, Torre T, Fearn PA, Leibel SA, Kattan MW. Potency after permanent prostate brachytherapy for localized prostate cancer. Int J Radiat Oncol Biol Phys 2001;50:1235–1242.
23. Merrick GS, Butler WM, Wallner KE, Murray BC, Allen Z, Galbreath RW. Influence of hormonal therapy on late rectal function after permanent prostate brachytherapy with or without supplemental external beam radiotherapy. Int J Radiat Oncol Biol Phys 2004;58:68–74.
24. Crook J, McLean M, Catton C, Yeung I, Tsihlias J, Pintilie M. Factors influencing risk of acute urinary retention after TRUS-guided permanent prostate seed implantation. Int J Radiat Oncol Biol Phys 2002;52:453–460.
25. Mols F, van de Poll-Franse LV, Vingerhoets AJ, Hendrikx A, Aaronson NK, Houterman S, Coebergh JW, Essink-Bot ML. Long-term quality of life among Dutch prostate cancer survivors: Results of a population-based study. Cancer 2006;107:2186–2196.
26. Mols F, Vingerhoets AJ, Coebergh JW, Vreugdenhil G, Aaronson NK, Lybeert ML, van de Poll-Franse LV. Better quality of life among 10-15 year survivors of Hodgkin's lymphoma compared to 5-9 year survivors: A population-based study. Eur J Cancer 2006;42:2794–2801.
27. Mols F, Aaronson NK, Vingerhoets AJ, Coebergh JW, Vreugdenhil G, Lybeert ML, van de Poll-Franse LV. Quality of life among long-term non-Hodgkin lymphoma survivors: A population-based study. Cancer 2007;109:1659–1667.

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Abbreviations Used

EORTC-QLQ = European Organization of Research and Treatment of Cancer Quality of Life Questionnaire
HRQOL = health-related quality of life
LHRH = luteinizing hormone-releasing hormone
PSA = prostate-specific antigen